Nonlesional epilepsy surgery: “Be wary of risks”

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American Epilepsy Society | Annual Meeting
Eisai, UCB Pharma, Sunovian, SK Bios, NINDS, Upsher Smith

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Lundbeck

Investigator

Consultant via JHU

SHARE vision safety board
Orrin Devinsky, MD: “Mistakes in Epilepsy Care:”
Importance of “framing”--communicating surgical risks:

**Failure to Understand Framing**

- “Surgery is 99.95% safe” is very different than “Someone died from surgery” or “1 in 1500 die”.
  - Substitute benign brain tumor for epilepsy surgery
- Mentally invert presentations to better understand pros and cons
- Patients must trust their doctors, but they must also assess their doctor’s bias
- The neurosurgeon, the radiation oncologist & the neuro-oncologist
Similar patient with successful surgery:
30 year old man
Simple partial seizures since age 5 y
  twisting/posturing of left arm
  multiple daily episodes
  hand and finger movements
Eyes
Mouth
Tongue
Head
Arm
Hand
Fingers
Thumb
Trunk
Toes

Movement
Motor inhibition
Sensation

Ictal EEG onset
Spread
Motor recovery following MST
30 y/o RH male: motor SPS left hand/arm
Assessing nonlesional epilepsy surgery in medication-resistant epilepsy

1. Feasibility after initial screening: Uncertain
   – Scalp EEG and MRI non-localizing
   – Ictal onset zone likely to involve arm motor region

2. Alternative therapies available: YES
   – Newer effective AEDs not tried (LCM; TOP, investigational)
   – Neuropace stimulation?

3. Anticipated surgery: Possible
   – Combined multiple subpial transection (MST) & resection
   – Predicted seizure free outcome: ≤ 50%

4. Functional improvement with surgery: Uncertain
   – work as a chef: risks with loss of arm/hand coordination
   – independence with driving, housing, etc. unlikely with palliative surgery
Remaining effective AEDs available for patient*: Prospective audits with adjunctive new AEDs in localisation-related epilepsies: 2013

<table>
<thead>
<tr>
<th>Audit</th>
<th>N=</th>
<th>Seizure-free (%)</th>
<th>Responders (%)*</th>
<th>Marginal Response(%)**</th>
<th>Withdrawn (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topiramate</td>
<td>135</td>
<td>28 (20.7) *</td>
<td></td>
<td>65 (48.2) *</td>
<td>42 (31.1)</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>136</td>
<td>32 (23.5)</td>
<td>28 (20.6)</td>
<td>32 (23.5)</td>
<td>44 (32.4)</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>141</td>
<td>18 (12.8)</td>
<td>21 (14.9)</td>
<td>43 (30.5)</td>
<td>59 (41.8)</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>135</td>
<td>14 (10.4)</td>
<td>33 (24.4)</td>
<td>20 (14.8)</td>
<td>68 (50.4)</td>
</tr>
<tr>
<td>Lacosamide</td>
<td>160</td>
<td>35 (21.9) *</td>
<td>35 (21.9)</td>
<td>54 (33.7) *</td>
<td>36 (22.5)</td>
</tr>
</tbody>
</table>

* Martin J Brodie, Kevin Kelly, Linda J Stephen
Epilepsy Unit, Division of Cardiovascular and Medical Sciences,
Western Infirmary, Glasgow, Scotland, UK
Epilepsy surgery outcomes in patients with normal preoperative MRI: N=24
(7 of 9 with FLE had cortical dysplasia pathology)
(2.9% of all surgery patients)

Chapman K et al. J Neurol Neurosurg Psychiatry 2005;76:710-713
16% of patients with focal cortical dysplasia in epilepsy surgery series had histories of head trauma

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 55)</th>
<th>Dual pathology (N = 31)</th>
<th>Isolated FCD (N = 24)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (seizures/month)</td>
<td>32.4</td>
<td>20.6</td>
<td>47.5</td>
<td>0.28</td>
</tr>
<tr>
<td>Family history of seizures (%)</td>
<td>27</td>
<td>30</td>
<td>29</td>
<td>0.69</td>
</tr>
<tr>
<td>Febrile seizures (%)</td>
<td>9</td>
<td>13</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Epilepsy (%)</td>
<td>18</td>
<td>13</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Febrile seizures (%)</td>
<td>16</td>
<td>16</td>
<td>17</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Head trauma (%)</strong></td>
<td><strong>16%</strong></td>
<td><strong>16</strong></td>
<td><strong>17</strong></td>
<td><strong>1.0</strong></td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>CNS infections (%)</td>
<td>11</td>
<td>19</td>
<td>0</td>
<td>0.03</td>
</tr>
<tr>
<td>No risk factors (%)</td>
<td>44</td>
<td>39</td>
<td>50</td>
<td>0.089</td>
</tr>
</tbody>
</table>

Bautista JF. Epilepsy Research 2003
Bilateral fronto-temporal intracranial strip localization: JHU

Table 2. Univariate analysis: strong correlations between seizure etiology, focal MRI and successful surgery (Engel Class I, II, III).

<table>
<thead>
<tr>
<th>Successful surgery</th>
<th>Chi-square</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Symptomatic seizure etiology</td>
<td>5.06</td>
<td>0.024</td>
</tr>
<tr>
<td>Focal MRI findings</td>
<td>5.06</td>
<td>0.024</td>
</tr>
<tr>
<td>Focal seizures on strip EEG</td>
<td>18.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Etiology &amp; MRI findings</td>
<td>12.5</td>
<td>0.028</td>
</tr>
<tr>
<td>Scalp &amp; strip VEEG correlation</td>
<td>3.4</td>
<td>.065</td>
</tr>
</tbody>
</table>

• Ictal localization on strip recordings:
  • Focal: 27 (54%)
  • Multifocal or nonlocalized: 23 (46%)
  • Limited correlation between scalp/strip VEEG

• Surgery outcome:
  • 27 (54%) patients had resective surgery
  • After surgery 85% improved (Engel Class I, II, III); 48% seizure-free.
Frontal lobe scalp and subdural EEG localization of ictal seizure onset often differ

Frontal lobe ictal seizure onset focus, N=15

<table>
<thead>
<tr>
<th>Scalp recordings</th>
<th>Subdural recordings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>Often extensive onset</td>
</tr>
<tr>
<td>Poorly localized</td>
<td>May be localized</td>
</tr>
<tr>
<td>Either</td>
<td>Majority extensive onset (=1/3 complete resection)</td>
</tr>
</tbody>
</table>

Vicenta Salanova, Arch Neurology 1993
Optimizing ictal recordings for presumed FLE:

1) Consider adding 10% system frontal electrodes (not temporal).
2) Do not link adjacent 10% leads (unable to detect voltage gradients).
3) Use additional display montages to identify broad frontal sources:
   • Transverse bipolar
   • Contralateral distant reference (e.g. P7)
   • Average reference
Significant risks with subdural grid electrodes

11 of 91 (12%) with infections following SGE recording
Hersh, EH. J Neurosurgery 2013

Surgical complications in 6.6% (1.5% permanent) Van Gompel, JJ. Neurosurgery 2008

<table>
<thead>
<tr>
<th>Complications, no. (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Empyema</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Abscess</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Hematoma</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>9 (4.5)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Permanent deficit</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
Significant risks with extratemporal resections
Hader, WJ. Epilepsia, 2013

• Rate of minor and major medical complications: 6.1% and 1.1% respectively.
• Rate of minor and major neurologic complications: 11.9% and 6.5% respectively

<table>
<thead>
<tr>
<th>Major neurologic complications</th>
<th>Total</th>
<th>238</th>
<th>4.7 (4.1–5.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric only</td>
<td>957</td>
<td>49</td>
<td>5.1 (3.9–6.7)</td>
</tr>
<tr>
<td>Adults only</td>
<td>1,071</td>
<td>35</td>
<td>3.3 (2.4–4.5)</td>
</tr>
<tr>
<td>Temporal</td>
<td>3,358</td>
<td>138</td>
<td>4.1 (3.5–4.8)</td>
</tr>
<tr>
<td>Extratemporal</td>
<td>1,014</td>
<td>66</td>
<td>6.5 (5.2–8.2)</td>
</tr>
</tbody>
</table>

• Common medical and neurological complications in extratemporal resections:
  • Cerebrospinal fluid leak (3.6%)
  • Infection (3.2%)
  • Intracranial hematoma (3.1%)
  • Minor hemiparesis (7.9%)
  • Major hemiparesis (1.8%)
  • Minor field deficit (7.2%)
Conclusion: Pre-surgical counseling

• Alternative AED treatments available
  – Approx. 40% odds marked seizure reduction
  – seizure freedom not likely

• Risks from resective surgery are high:
  – 6% permanent deficit in extratemporal series
  – 10% deficit requiring treatment ("minor hemiparesis")
  – Peri-rolandic surgery: risk of deficit >40%

• Chances of success with surgery are moderate
  – 40% seizure free (if resection/MST feasible)
  – 30% seizure reduction

• Determine individual patient goals/decision
Case: rebuttal & conclusion

– Contentious epilepsy surgery conference: one stage monitoring with large right frontal grid

– Seizures pause for 4 days after implant surgery with anesthesia. AEDs dropped: cluster of 2 SPS and then 3 2TC seizures.

– Intracranial recording & stimulation correspond to SPS-motor episodes with ictal seizure onset in motor and premotor cortex
Case: Likely outcome

Seizure onset over a right posterior frontal region

- Includes motor and premotor cortex
- Multiple subpial transection in motor cortex & premotor region resection considered
- Patient accepts surgery: nonspecific pathology detected
- **Estimated Outcome:** mild left arm paresis, weekly milder seizures, trying new AEDs, works as a caterer, not a chef